For Clinicians Requesting Peramivir IV for Hospitalized Patients with H1N1 Influenza

Enclosed are instructions (pages 1-3) and form (pages 4-9) for requesting Peramivir IV under FDA-issued Emergency Use Authorization (EUA).

Please read this document and fax your request for Peramivir IV as directed.

You must:

1) read the FDA-issued Emergency Use Authorization Fact Sheet for Healthcare Providers (www.cdc.gov/h1n1flu/eua)

2) certify that you understand and agree to the terms and conditions of authorized use of Peramivir IV under the FDA-issued Emergency Use Authorization (EUA)

3) provide CDC with contact and location information for you and the hospital pharmacy that will receive the requested Peramivir IV

You must provide a completed form with all requested information before CDC can process your request.

FAX this completed request form to (770) 488-7107 or (404) 553-7508.

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Clinicians Considering the Use of Peramivir IV

Currently there is no intravenous formulation of antiviral product approved by the U.S. Food and Drug Administration (FDA) for the treatment of hospitalized patients with influenza. Peramivir, a neuraminidase inhibitor, is an **unapproved (investigational)** antiviral drug available in an intravenous (IV) formulation. Peramivir IV is currently under development for treatment of acute influenza in patients who require hospitalization due to the severity of influenza virus infection. The efficacy and safety of Peramivir have not yet been established. The FDA has issued an Emergency Use Authorization (EUA) to allow use of Peramivir IV to treat certain adult and pediatric patients with suspected or laboratory confirmed 2009 H1N1 virus infection or infection due to nonsubtypable influenza A virus suspected to be H1N1 based on community epidemiology. The authorized use of Peramivir IV under EUA is subject to the scope, conditions, and terms of FDA-issued EUA.

Clinicians considering Peramivir IV under EUA must read and understand the content of the FDA-issued Emergency Use Authorization of Peramivir IV: Fact Sheet For Health Care Providers (www.cdc.gov/h1n1flu/eua) prior to initiating a request and must agree to comply with terms and conditions of authorized use of Peramivir IV per the FDA-issued EUA in order to successfully complete and transmit the request for this product.

Additionally, clinical studies of Peramivir IV in hospitalized patients are currently being conducted. Clinicians who wish to consider whether their patients would be appropriate for inclusion in those studies, please refer to http://www.ClinicalTrials.gov for more information on these trials.

If, after reviewing these and other materials on the CDC website, you have clinical questions relating to use of Peramivir IV, please contact CDC INFO at 1-800-232-4636, 24 hours a day, 7 days a week. (For TTY, call 1-888-232-6348.)

If, after reviewing these materials, you would like to proceed with requesting Peramivir IV, please complete this request form.

If, after reviewing these materials, you have questions relating to emergency use authorizations, contact: EUA.OCET@fda.hhs.gov.

Other Antiviral Treatment Options for Patients Hospitalized due to Complicated Influenza

Currently there is no FDA-approved intravenous formulation of antiviral product for the treatment of hospitalized patients with influenza. Oral Tamiflu® (oseltamivir) and inhalation Relenza® (zanamivir) are FDA-approved for the treatment of uncomplicated acute illness due to influenza. Use of

these medications is authorized for emergency use for the treatment of hospitalized patients with 2009 H1N1 influenza under FDA-issued EUAs.

The FDA-issued EUA for Tamiflu® authorizes the use of Tamiflu® for the treatment of patients hospitalized due to complicated influenza and in patients symptomatic for more than 2 days, including pediatric patients less than 1 year old. The authorized use of Tamiflu® is subject to the terms and conditions of the EUA. For more information on the Tamiflu® EUA, please see: www.cdc.gov/h1n1flu/eua/tamiflu.htm.

The FDA-issued EUA for Relenza® authorizes use of Relenza® for the treatment of patients hospitalized due to complicated influenza and in patients symptomatic for more than 2 days. The authorized use of Relenza® is subject to the terms and conditions of the EUA. For more information on the Relenza EUA, please see: www.cdc.gov/h1n1flu/eua/relenza.htm.

You will be required to acknowledge your compliance with the terms and conditions of the EUA in order to obtain Peramivir IV.

Submitting Your Request for Peramivir IV

The next six pages contain a series of questions or statements for your review and acknowledgement, and a form requesting contact and locator information for you and the hospital to which the Peramivir IV will be shipped.

You must answer or acknowledge your understanding of all requested items, and you must provide all contact and locator information required. We will use the contact and locator information to contact you (or the hospital pharmacy) if we have questions about your request. We will also verify the shipping address you provide on page 8 of the enclosed form regarding the delivery of the drug. If we cannot reach you to verify shipping information or to resolve questions, the drug will not be shipped.

Please fax all six pages to (770) 488-7107 or (404) 553-7508.

Once a request for Peramivir IV is transmitted to CDC, you will be notified via email when product is approved for shipment. It may take up to 24 hours, once the decision to ship the product to you is made, for you to receive the drug at your hospital pharmacy/identified delivery location. Peramivir IV (200 mg/ 20 mL) is packaged as a box of 5 single-use vials.

Please FAX Completed Peramivir IV Request Form (pages 4-9) to: (770) 488-7107 or (404) 553-7508

Peramivir IV Request Form

Please acknowledge by marking an "X" on the line after each "Yes" or "Agree" that you have read, understand and agree to all statements below.

I am the treating clinician, and I certify my understanding of, and agree to, the following mandatory requirements for Peramivir IV administration under Emergency Use Authorization as specified in the "Emergency Use Authorization of Peramivir IV: Fact Sheet for Health Care Providers":	
Yes ____	Based on the available data, this patient has suspected or laboratory confirmed 2009 H1N1 virus infection or infection due to nonsubtypable influenza A virus suspected to be 2009 H1N1 based on community epidemiology.
Yes ____	This patient is admitted to a hospital and under the care or consultation of a licensed clinician (skilled in the diagnosis and management of patients with potentially life-threatening illness and the ability to recognize and manage medication-related adverse events).
Yes ____ Not Applicable _____ (Pediatric patient)	Peramivir IV is authorized for hospitalized adult patients for whom therapy with an IV agent is clinically appropriate, based upon one or more of the following reasons: i) patient not responding to either oral or inhaled antiviral therapy, or ii) drug delivery by a route other than IV (e.g. enteral oseltamivir or inhaled zanamivir) is not expected to be dependable or is not feasible, or iii) the clinician judges IV therapy is appropriate due to other circumstances.
Yes ____ If you marked "yes" here, you must calculate the dose required for your patient. Refer to the last page of this document for the information you need to calculate the dose. Not Applicable ____ (Adult patient)	Peramivir IV is authorized for hospitalized pediatric patients for whom an IV agent is clinically appropriate because: i) patient not responding to either oral or inhaled antiviral therapy, or ii) drug delivery by a route other than IV (e.g. enteral oseltamivir or inhaled zanamivir) is not expected to be dependable or is not feasible. The formula to calculate the age-ranged, weight-based dose is found on page 9 of this document. Please be sure to complete the calculation on page 9.
Agree ____	Health Care Providers (to the extent practicable given the circumstances of the emergency) must document in the patient's medical record that the patient/caregiver has been: i) given the Fact Sheet for Patients and Parents/Caregivers, ii) informed of alternatives to receiving authorized Peramivir IV, and iii) informed that Peramivir IV is an unapproved drug that is authorized for use under Emergency Use Authorization.
Agree ____	Patients with known or suspected renal insufficiency must have creatinine clearance determined prior to Peramivir IV dose calculation and first administration.

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Agree _____	Patients with history of severe allergic reaction to any other neuraminidase inhibitor (zanamivir or oseltamivir) or any ingredient of Peramivir IV must not receive Peramivir IV.
Agree _____	The prescribing health care provider and/or their designee is/are responsible for mandatory responses to requests from FDA, CDC or their designee for information about adverse events and medication errors following receipt of Peramivir IV. For example, health care providers and/or their designee will be asked whether Peramivir IV was administered, if a selected adverse event or medication error occurred, and if the adverse event or medication error was reported to FDA MedWatch.
Agree _____	The prescribing health care provider and/or their designee is/are responsible for mandatory FDA MedWatch reporting of all medication errors and selected adverse events occurring during Peramivir IV treatment within 7 calendar days from the onset of the event. Selected adverse events are death; neuropsychiatric events; renal adverse events; serious skin adverse events (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis); hypersensitivity reactions adverse events (e.g., anaphylaxis, urticaria, angioedema); severe IV site or IV administration adverse events (e.g., septic phlebitis, infiltrated IV); or other serious adverse events. Serious Adverse Events are defined as: any life-threatening adverse drug experience that may prolong existing hospitalization, result in a persistent or significant disability/incapacity or a congenital anomaly or birth defect or an event that may jeopardize the patient to an extent that may require medical/surgical intervention to prevent one of the outcomes above including death.

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The following considerations, as specified in the "Emergency Use Authorization of Peramivir IV: Fact Sheet for Health Care Providers," should be considered prior to administering Peramivir IV (these are not mandatory requirements for use). I certify that I have reviewed the following FDA recommendations for use:	
	Data Available on Safety and Efficacy:
Agree ____	The efficacy and safety of Peramivir IV (or the other approved neuraminidase inhibitors) have not been established in hospitalized patients with any type of influenza A or B virus including 2009 H1N1 virus.
Agree ____	Results from the phase 2 and 3 trials with IV and intramuscular (IM) administration include a statistically significant effect of a single 300 mg or 600 mg IV dose of Peramivir compared to placebo in adult patients with acute uncomplicated influenza. Additionally, three phase 2 trials and one phase 3 trial, including one trial in hospitalized patients, did not show statistically significant treatment differences between Peramivir and placebo or oseltamivir.
Agree ____	Approximately 1,891 persons in clinical trials subjects have received Peramivir given IV or IM, including 478 who received a single dose of 600 mg IV. Data on multi-dose administration are limited with 33 adult clinical trial subjects who received approximately 600 mg (or higher) intravenously once daily for five or more days.
Agree ____	No pediatric patients (age < 18 years) have received Peramivir in clinical trials. No pharmacokinetic, safety or efficacy data are available in the pediatric population. However, limited use of Peramivir IV in children has been allowed for Peramivir IV 600 mg once daily for 5 to 10 days under emergency IND procedures.
Agree ____	Limited safety data from adults are available on Peramivir IV use for 5 days or longer. However, limited use of Peramivir IV in adults has been allowed for Peramivir IV 600 mg once daily for 5 to 10 days under emergency IND procedures.
Agree ____	Peramivir has not been administered to pregnant women or nursing mothers in clinical trials. No pharmacokinetic, safety or efficacy data are available in pregnant women or nursing mothers.
Agree ____	Use of Peramivir has not been shown to reduce the risk of transmission of influenza to others.
	Treatment Regimens and Timeliness:
Agree ____	Empiric antiviral treatment of hospitalized patients with suspected influenza should not be delayed pending laboratory confirmation of influenza because antiviral treatment is most effective when initiated as early as possible. In addition, a negative influenza antigen test (rapid influenza diagnostic test or immunoflorescence) does not rule out influenza virus infection.
Agree ____ Select the course of treatment you are requesting: ___ 5-day ___ 10-day	Initial treatment courses of 5 days or 10 days are permitted. Patients with critical illness (for example, those with respiratory failure or those requiring intensive care unit admission) might benefit from a longer treatment course, although there are no available data demonstrating that longer treatment courses are more effective. Limited data are available on the use of Peramivir IV for up to 10 days or longer.
Agree ____	Peramivir IV can be used at any time after onset of symptoms in hospitalized patients; however, no data are available regarding initiation of Peramivir IV beyond 72 hours after symptom onset.

	Drug Resistance:
Agree ____	2009 H1N1 virus strains circulating worldwide are susceptible to the neuraminidase inhibitor class of antivirals (oseltamivir, zanamivir, Peramivir IV), and resistant to the adamantane class (amantadine, rimantadine). Rare, sporadic cases of oseltamivir-resistant virus infection associated with the H275Y mutation in the neuraminidase have been reported, including in the United States. To date, there is no evidence worldwide of on-going community-wide transmission of oseltamivir-resistant 2009 H1N1 virus. The latest antiviral resistance surveillance data for the United States can be found at: http://www.cdc.gov/flu/weekly/.
Agree ____	Peramivir IV should not be used for treatment of 2009 H1N1 virus infection in patients with documented or highly suspected oseltamivir resistance.
Agree ____	Peramivir IV should be used with caution in patients with documented (neuraminidase E119D or R292K) or highly suspected zanamivir resistance. The activity of Peramivir IV against zanamivir resistant virus is unknown.
Agree ____	Limited data are available on the combination antiviral activity relationships of Peramivir with oseltamivir. No data are available on the combination antiviral drugs, although combination of Peramivir with oseltamivir in a mouse influenza A virus challenge study demonstrated additive antiviral activity compared to use of a single agent alone. The clinical significance of these data is unknown.
Agree ____	**By submitting this request for Peramivir IV, I agree to the preceding considerations, recommendations, and mandatory requirements and understand that they do not replace or supersede in part or whole any component of the Peramivir IV EUA. As the treating clinician prescribing Peramivir IV for the treatment of my patient in my care, I am responsible for understanding and complying with the terms and conditions of the FDA-issued EUA for Peramivir IV.**

Please FAX Completed Peramivir IV Request Form (pages 4-9) to: (770) 488-7107 or (404) 553-7508

Required Information for Submission of Peramivir IV Request

This request is for an adult patient_____ or a pediatric patient_____ (age = _____)

Are you requesting Peramivir IV for a 5 day _____ or 10 day _____ course of treatment?
(If this is an adult patient, you will receive 15 vials of drug in 3 boxes for a 5 day course; 30 vials in 6 boxes for a 10 day course. Peramivir IV (200 mg/ 20 mL) is packaged as a box of 5 single-use vials.)

If this is a pediatric patient you must specify the number of vials _____ and number of boxes _____ you are requesting (**See next page for dosing calculation for pediatric patients**).

Licensed Clinician Requesting Peramivir IV

First and Last Name _____
Professional Degree _____ **(MD, DO, PA or NP)**
Hospital _____
Cell Phone (____) _____-_____
Pager Number (____) _____-_____ **FAX Number** (____) _____-_____
Email address _____

Hospital Receiving Peramivir IV

Person responsible for receiving Peramivir IV
First and Last Name _____
Job Title (e.g. pharmacist) _____
Email address _____

Shipping Address (where Peramivir shipment will be received)*
Street Address _____
Building, room number _____
City _____
State, Zip Code _____
Phone Number (____) _____-_____**ext** _____
FAX Number (____) _____-_____

Identified person/hospital pharmacy must be able to receive delivery of product 24 hours a day, 7 days a week.

Shipment and Delivery Notice:

Once a request for Peramivir IV is transmitted to CDC, you will be notified via email when product is approved for shipment. It may take up to 24 hours, once the decision to deploy product to you is made, for you to receive the drug at your hospital pharmacy/identified delivery location.

Please FAX Completed Peramivir IV Request Form (pages 5-9) to: (770) 488-7107 or (404) 553-7508

Required Information for Submission of Request for Peramivir IV for a Pediatric Patient

Pediatric dosing is age-ranged, weight-based dosing as indicated in the table below. You must know your patient's age and weight in kilograms.

Pediatric Dosage Recommendations*		
My Patient's Age	**Age**	**Dose**
	Birth through 30 Days	6 mg/kg
	31 Days through 90 Days	8 mg/kg
	91 Days through 180 Days	10 mg/kg
	181 Days through 5 Years	12 mg/kg
	6 Years through 17 Years	10 mg/kg

***Maximum Daily Dose is 600 mg**

Using the table above, the daily Peramivir IV dose:
Patient weight (kg)_____ x Age-based dose (mg/kg) _____ = Daily dose (mg/day) _____

Total Boxes Needed		
If Daily Dose is	**And intended treatment course is**	
	5 Day Course	**10 Day Course**
1-200 mg	1 Box	2 Boxes
201-400 mg	2 Boxes	4 Boxes
401-600 mg	3 Boxes	6 Boxes

Please circle the Total Boxes Needed that corresponds to the Daily Dose and the length of the treatment course for your patient and include the total boxes on the previous page.